

AMENDMENTS TO THE CLAIMS

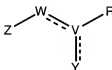
The following listing of the claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A method of inhibiting ~~dynamin activity~~~~dynamin-dependent endocytosis in cells, the method comprising treating the cells~~ contacting dynamin with an effective amount of a compound of formula I, or a physiologically acceptable salt thereof, wherein



Formula I

M and M' are each independently a moiety of formula II and are the same or different, and Sp is a spacer;



Formula II

V is C or CH;

W is CH or a linker group; and

Y is ~~hydrogen~~, cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, sulfur, or an unsubstituted C₁-C₃ group or C₁-C₃ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; or

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic or carbocyclic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the heterocyclic or carbocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, sulfur, or an unsubstituted C₁-C₃ group or

C₁-C₃ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R is CH₂R', CXR' or CHX'R';

X is O or S;

X' is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, or an unsubstituted C₁-C₃ group or C₁-C₃ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur;

R' is NH, O or S bonded to the spacer; and

Z is selected from:

(a) an unsubstituted heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S;

(b) an unsubstituted carbocyclic group consisting of one or two rings independently having 5 or 6 ring members;

(c) a heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S wherein the heterocyclic group has one or more substituents independently selected from:

(i) nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C₁-C₂ alkoxy and C₁-C₂ acyl; and

(ii) a C₁-C₂ alkyl or C₁-C₂ alkenyl group with at least one substituent selected from nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C₁-C₂ alkoxy and C₁-C₂ acyl; and

(d) a carbocyclic group consisting of one or two rings independently having 5 or 6 ring members, and at least two substituents when W is CH or a linker group or W, V and Y form an unsubstituted carbocyclic group, or at least one substituent when W, V and Y form a heterocyclic group, independently selected from:

(i) nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C₁-C₂ alkoxy and C₁-C₂ acyl; and

(ii) a C₁-C₂ alkyl or C₁-C₂ alkenyl group with at least one substituent selected from nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulfhydryl, C₁-C₂ alkoxy and C₁-C₂ acyl;

wherein when Z of one of M or M' is selected from (b), Z of the other of M or M' is selected from (a), (c) or (d).

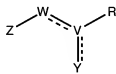
2-25. (Cancelled)

26. (Currently amended) A method of prophylaxis or therapeutic treatment of a disease or condition in a mammal mediated by dynamin-dependent endocytosis, the method comprising administering to the mammal an effective amount of a compound of Formula I ~~according to claim 1~~, or a physiologically acceptable salt, or prodrug thereof, wherein:

M-Sp-M'

Formula I

M and M' are each independently a moiety of formula II and are the same or different, and Sp is a spacer;



V is C or CH;

W is CH or a linker group; and

Y is cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, sulfur, or an unsubstituted C₁-C₃ group or C₁-C₃ group substituted with at

least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulphydryl, carboxy, thiocarboxy and sulfur; or

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic or carbocyclic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the heterocyclic or carbocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulphydryl, carboxy, thiocarboxy, sulfur, or an unsubstituted C₁-C₃ group or C₁-C₃ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulphydryl, carboxy, thiocarboxy and sulfur; and

R is CH₂R', CXR' or CHX'R';

X is O or S;

X' is cyano, nitro, amino, halo, hydroxy, sulphydryl, carboxy, thiocarboxy, or an unsubstituted C₁-C₃ group or C₁-C₃ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulphydryl, carboxy, thiocarboxy and sulfur;

R' is NH, O or S bonded to the spacer; and

Z is selected from:

(a) an unsubstituted heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S;

(b) an unsubstituted carbocyclic group consisting of one or two rings independently having 5 or 6 ring members;

(c) a heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S wherein the heterocyclic group has one or more substituents independently selected from:

(i) nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulphydryl, C₁-C₂ alkoxy and C₁-C₂ acyl; and

(ii) a C₁-C₂ alkyl or C₁-C₂ alkenyl group with at least one substituent selected from nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulphydryl, C₁-C₂ alkoxy and C₁-C₂ acyl; and

(d) a carbocyclic group consisting of one or two rings independently having 5 or 6 ring members, and at least two substituents when W is CH or a linker group or W, V and Y form an unsubstituted carbocyclic group, or at least one substituent when W, V and Y form a heterocyclic group, independently selected from:

(i) nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulphydryl, C₁-C₂ alkoxy and C₁-C₂ acyl; and

(ii) a C₁-C₂ alkyl or C₁-C₂ alkenyl group with at least one substituent selected from nitro, NH, amino, cyano, halo, hydroxy, carboxy, oxo, sulfur, sulphydryl, C₁-C₂ alkoxy and C₁-C₂ acyl;

wherein when Z of one of M or M' is selected from (b), Z of the other of M or M' is selected from (a), (c) or (d).

27-55. (Cancelled)

56. (Currently amended) ~~A compound~~ method according to claim [[55]] 26 wherein for at least one of M and M':

V is C;

W is CH; and

Y is ~~hydrogen~~, cyano, nitro, amino, halo, hydroxy, sulphydryl, carboxy, thiocarboxy, or an unsubstituted C₁-C₂ group or C₁-C₂ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulphydryl, carboxy, thiocarboxy and sulfur; or

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic or carbocyclic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the carbocyclic or heterocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulphydryl, carboxy, thiocarboxy and sulfur, or an unsubstituted C₁-C₂ group or C₁-C₂ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulphydryl, carboxy, thiocarboxy and sulfur; and

R is CH₂R', CXR' or CHX'R';

X is O or S; and

X' is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy, or an unsubstituted C₁-C₂ group or C₁-C₂ group substituted with at least one group independently selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl; carboxy, thiocarboxy and sulphur.

57. (Currently amended) A ~~compound~~ method according to claim 56 wherein:

Y is cyano, nitro, amino, carboxy, hydroxy, sulfhydryl, or thiocarboxy, ~~or a C₁-C₂ group substituted with a group selected from cyano, nitro, amino, hydroxy, sulfhydryl, carboxy and thiocarboxy;~~

W, V and Y form a 5 or 6 membered substituted or unsubstituted heterocyclic or carboxylic ring fused with Z, wherein the heterocyclic ring includes from 1 to 3 heteroatoms selected from O, N and S, and the carbocyclic or heterocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, amino, hydroxy, sulfhydryl, carboxy and thiocarboxy, or a C₁-C₂ group substituted with a group selected from cyano, nitro, amino, hydroxy, sulfhydryl, carboxy and thiocarboxy; and

R is CXR'.

58. (Currently amended) A ~~compound~~ method according to claim [[55]] 57 wherein the Z group is selected from:

[[i)] a heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms independently selected from O, N and S;

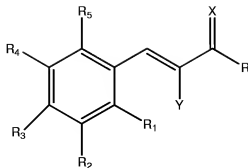
[[ii)] a heterocyclic group consisting of one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms independently selected from O, N and S, wherein the heterocyclic group has one or more substituents independently selected from nitro, NH, halo, cyano, amino, hydroxy, carboxy, oxo, sulfur, and C₁-C₂ alkoxy; and

[[iii)] an carbocyclic group consisting of one or two rings independently having 5 or 6 ring members, and at least two substituents independently selected from nitro, NH, amino, halo, cyano, hydroxy, carboxy, oxo, sulfur and C₁-C₂

alkoxy.

59. (Cancelled)
60. (Currently amended) A ~~compound~~ method according to claim [[55]] 58 wherein the Z group has ~~at least one of M and M' comprises:~~
at least two said substituents in ortho positions relative to one another on a said ring of Z or in adjacent substitution positions, when the Z group is a carbocyclic group selected from (d) and W is CH or a C₁-C₃-linker group; or
~~the, or one of, the a substituent~~ substituents on a carbon atom adjacent to the, ~~or one of the, a heteroatom of a said ring of Z, when the Z group is a heterocyclic group~~
~~heteroatom~~ [(s) when the Z group is a heterocyclic group selected from (e); or
when W, V and Y are cyclised forming a heterocyclic ring fused with Z, ~~the, or one of, the substituents~~ a substituent on a carbon atom of a said ring of the Z group, the carbon atom being at least one bond length from the heterocyclic ring formed by W, V, and Y spaced at least one bond length from the heterocyclic ring.
61. (Currently amended) A ~~compound~~ method according to claim [[55]] 60 wherein the Z group consists of a single aryl side ring of 5 or 6 members ~~when the Y substituent of one of M or M' is hydrogen, the Y substituent of the other of M and M' is other than hydrogen.~~
62. (Currently amended) A ~~compound~~ method according to claim [[55]] 61 wherein W, V and Y form a [[5 or]] 6 membered heterocyclic ring fused with Z.
63. (Currently amended) A ~~compound~~ method according to claim [[62]] 61 wherein V is C₁, W is CH and Y is cyano ~~the heterocyclic ring fused with Z forms a two ring heterocyclic group.~~

64. (Currently amended) A ~~compound~~ method according to claim [[55]] 58 wherein ~~the Z group is~~ comprises an aryl group consisting of one or two rings independently having 5 or 6 ring members, and at least two substituents independently selected from nitro, NH, amino, halo, cyano, hydroxy, carboxy, oxo, sulphur and C₁-C₂ alkoxy.
65. (Currently amended) A ~~compound~~ method according to claim 64 wherein ~~the Z group is~~ comprises an aryl group ~~consisting of one ring~~ a phenyl group having 6 ring members and at least two substituents independently selected from nitro, amino, halo, cyano, hydroxy, carboxy and C₁-C₂ alkoxy.
66. (Currently amended) A ~~compound~~ method according to claim 65 wherein the aryl phenyl group has at least two substituents independently selected from nitro, amino, carboxy and hydroxy.
67. (Currently amended) A ~~compound~~ method according to claim [[55]] 58 wherein ~~the Z group is~~ comprises a heterocyclic group having one or two rings independently having 5 or 6 ring members including up to 3 heteroatoms selected from O, N and S, wherein the heterocyclic group has one or more substituents independently selected from nitro, NH, halo, cyano, amino, hydroxy, carboxy, oxo, sulphur and C₁-C₂ alkoxy.
68. (Currently amended) A ~~compound~~ method according to claim 67 wherein the heterocyclic group has one or more substituents independently selected from nitro, amino carboxy and hydroxy.
69. (Currently amended) A ~~compound~~ method according to claim [[55]] 26 wherein M and M' are each independently a moiety as follows:



wherein: X is O or S ;

Y is cyano, nitro, amino, halo, hydroxy, sulfhydryl, carboxy, or thiocarboxy; or

R₁ and Y are cyclised forming a 5 or 6 membered substituted or unsubstituted heterocyclic or carbocyclic ring, wherein the heterocyclic ring includes 1 or 2 heteroatoms selected from O, N and S, and the carbocyclic or heterocyclic ring, when substituted, has at least one substituent selected from cyano, nitro, NH, amino, oxo, halo, hydroxy, sulfhydryl, carboxy, thiocarboxy and sulfur; and

R₂ to R₅ are independently hydrogen or a substituent independently selected from nitro, amino, halo, hydroxy, carboxy, sulfhydryl, thiocarboxy, C₁-C₂ alkoxy and C₁-C₂ acyl; or

~~R₂ to R₅ are independently hydrogen or a substituent independently selected from nitro, amino, halo, hydroxy, carboxy, sulfhydryl, thiocarboxy, halo, C₁-C₂ alkoxy and C₁-C₂ acyl; and~~

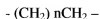
R₁ to R₅ are independently hydrogen or a substituent independently selected from nitro, amino, halo, hydroxy, carboxy, sulfhydryl, thiocarboxy, halo, C₁-C₂ alkoxy and C₁-C₂ acyl; and

R is NH, O is S bonded to the spacer Sp; and

wherein at least one of M and M' is characterised in that, at least two of R₁ to R₅[[.]] are other than hydrogen, and when R₁ to R₂ are other than hydrogen at least one of R₃ to R₅ is also other than hydrogen, or when R₁ and Y are cyclised, at least two of R₂ to R₅ are other than hydrogen when R₁ and Y form an unsubstituted carbocyclic group or at least one of R₂ to R₅ is other than hydrogen when Y and R₁ form a heterocyclic group.

70. (Currently amended) A ~~compound~~ method according to claim 69 wherein at least two of R_1 to $[[R_3]]$ R_5 are other than hydrogen.
71. (Currently amended) A ~~compound~~ method according to claim $[[69]]$ 70 wherein at least two of R_1 to R_5 are in ortho positions relative to one another.
72. (Currently amended) A ~~compound~~ method according to claim $[[69]]$ 71 wherein at least three of R_1 to R_5 are other than hydrogen and are in one of M and M' has three substituents and wherein the substituents are adjacent substitution positions to one another.
73. (Currently amended) A ~~compound~~ method according to claim 72 wherein at least two of R_2 to R_4 are hydroxy either ~~R_1 to R_3 are other than hydrogen or R_2 to R_5 are other than hydrogen.~~
74. (Currently amended) A ~~compound~~ method according to claim $[[69]]$ 70 wherein when at least one said substituent of R_1 to R_3 or R_2 to R_5 is halo, C_1 - C_2 alkoxy or C_1 - C_2 acyl, at least one other said substituent is selected from nitro, amino, hydroxy, carboxy and thiocarboxy when R_1 and Y are cyclised and form a heterocyclic ring, or at least two other said substituents are selected from nitro, amino, hydroxy, carboxy and thiocarboxy when R_1 and Y are not cyclised or form an unsubstituted carboxylic ring.
75. (Currently amended) A ~~compound~~ method according to claim $[[69]]$ 73 wherein Y is cyano, X is O and R is NH.
76. (Currently amended) A ~~compound~~ method according to claim $[[55]]$ 75 wherein M and M' are the same.
77. (Currently amended) A ~~compound~~ method according to claim $[[55]]$ 26 wherein the spacer Sp permits the compound to adopt a hairpin conformation.

78. (Currently amended) A ~~compound~~ method according to claim [[55]] 26 wherein the spacer Sp comprises an unsubstituted alkane chain as follows:



wherein n is an integer of from 1 to 5.

79. (Currently amended) A ~~compound~~ method according to claim 1 wherein the compound of Formula I is a dimeric tyrphostin.
80. (Currently amended) A method according to claim 26 wherein the compound of Formula I is a dimeric tyrphostin ~~pharmaceutical composition comprising a compound as defined in claim 55 together with a physiologically acceptable excipient, carrier or diluent.~~
81. (New) A method according to claim 73 wherein X is O, R is NH and R₁ and Y are cyclised, forming a substituted heterocyclic group with 6 ring members.
82. (New) A method according to claim 26 wherein the disease or condition is selected from the group consisting of cancers, ophthalmologic diseases, immunodeficiency diseases, gastrointestinal diseases, pathogenic infections, kidney diseases, epilepsy, diseases or conditions associated with cell vesicle trafficking, diseases or conditions characterized by synaptic signal transmission, and neurological, neurodegenerative and nervous system diseases and conditions.
83. (New) A method according to claim 81 wherein the disease or condition is selected from the group consisting of neurological, neurodegenerative and nervous system disease and conditions.
84. (New) A method according to claim 82 wherein the disease or condition is associated with cell vesicle trafficking or is characterized by synaptic signal transmission.

85. (New) A method according to claim 81 wherein the disease or condition is epilepsy.
86. (New) A method according to claim 1 being a method for inhibiting dynamin-dependent endocytosis in cells, the method comprising treating the cells with an effective amount of the compound of formula I, or a physiologically acceptable salt or prodrug thereof.